Prenatal Environmental Exposures and Child Health and Development: Insights From a NYC Cohort Study

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and
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Mission: Prevention of childhood asthma, neurodevelopmental impairment, obesity and cancer through early identification of environmental risk factors and translation to intervention
CCCEH: Parallel Studies of In Utero Exposures and Childhood Disease

New York City, USA (1998-present)
N. Manhattan/S. Bronx Cohort
725 mothers & newborns and 100+ siblings

World Trade Center Cohort
329 mothers & newborns

Krakow, Poland (2000-present)
550 mothers & newborns

Chongqing and Taiyuan, China
(2001-present)
~800 mothers & newborns

Asthma
Obesity/metabolic disorders
Neurodevelopment
Cancer Risk

Adult Diseases

Perera, 2012
THE GROWING BURDEN OF ADVERSE BIRTH OUTCOMES, NEURODEVELOPMENTAL DISORDERS AND DISEASE IN CHILDREN

• 8% of U.S. babies born low birth weight; 14% of African American babies

• 12% of children in the United States ages 3 to 17 years are affected by neurodevelopmental disorders such as ADHD, learning disorders, or intellectual disability.

• 13.6% of US children have been diagnosed with asthma

• 17% of US children and adolescents aged 2—19 years are obese
The Growing Burden of Adverse Birth Outcomes, Neurodevelopmental Disorders and Disease in Children

• 8% of U.S. babies born low birth weight; 14% of African American babies
• 12% of children in the United States ages 3 to 17 years are affected by neurodevelopmental disorders such as ADHD, learning disorders, or intellectual disability.
• 13.6% of US children have been diagnosed with asthma
• 17% of US children and adolescents aged 2—19 years are obese
• Rates of all these conditions have increased in recent decades
• We are all exposed but disproportionately high rates of illness in underserved communities
• Complex multifactorial diseases; environmental factors are known or suspected to contribute and are preventable
MULTIPLE ENVIRONMENTAL EXPOSURES OCCUR DURING PREGNANCY AND EARLY CHILDHOOD

- PAH/air pollution
- Pesticides
- BPA
- Phthalates
- Metals
- ETS
Prenatal exposures can have consequences throughout the life course

<table>
<thead>
<tr>
<th>Prenatal Exposure</th>
<th>Birth</th>
<th>Child</th>
<th>Adolescent</th>
<th>Adult</th>
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<tbody>
<tr>
<td>Metals: lead</td>
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<tr>
<td>mercury</td>
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<tr>
<td>arsenic</td>
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<tr>
<td>PAH/air pollution</td>
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<td>Pesticides: CPF</td>
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<td>Fungicides: vinclozolin</td>
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<tr>
<td>Chemicals: BPA</td>
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<tr>
<td>phthalates</td>
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<tr>
<td>Diet: folate deficiency</td>
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<td>nutrient deficiency</td>
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<td>Environ. tobacco smoke</td>
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</table>

[Animal and/or human evidence]
MECHANISMS BY WHICH IN UTERO EXPOSURES CAN AFFECT FETAL DEVELOPMENT

1. Genotoxicity: DNA damage and mutation
2. Oxidative Stress
3. Epigenetic alterations
4. Interference with normal hormonal pathways to disrupt the endocrine system
5. Gene-environment interactions
The CCCEH Cohort Study

Multiple exposures: multiple outcomes

- Birth Outcomes
- Neurodevelopment
- Obesity/metabolic disorders
- Asthma
- Cancer risk markers

PAH

BPA  Phthalates
Pesticides (CPF, pyrethroids)
PBDEs  Metals  ETS
ROLE OF EPIGENETIC MECHANISMS

Epigenetic Marks (CpG methylation) in cord blood

- PAH
- BPA, Phthalates
- Pesticides (CPF, pyrethroids)
- PBDEs, Metals, ETS

- Birth Outcomes
- Neurodevelopment
- Obesity/metabolic disorders
- Asthma
- Cancer risk markers
# Pregnancy Through Childhood: Repeat Measures on Women and Children

<table>
<thead>
<tr>
<th>SES/Exposure Assessment</th>
<th>Biomarkers of Exposure/Effect/Susceptibility</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Monitoring</td>
<td>Pesticides</td>
<td>Neurobehavioral Development</td>
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<td>Questionnaire</td>
<td>Cotinine</td>
<td>Asthma</td>
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<td>SES</td>
<td>Lead, mercury</td>
<td>Obesity/metabolic disorders</td>
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<td>Psychosocial stressors</td>
<td>PAH-DNA Adducts, PAH metabolites</td>
<td>Cancer Risk (chromosomal abnormalities)</td>
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<tr>
<td>GIS</td>
<td>BPA</td>
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<td>Phthalates</td>
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<td>Chromosomal Aberrations</td>
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<td>Immune Changes</td>
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<td>DNA methylation, Gene Expression</td>
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<td>Genetic Polymorphisms</td>
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<td>Antioxidants</td>
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The Mother and Fetus are Exposed to Multiple Toxicants (NYC)

Air Monitoring/Questionnaire:

- 100% of pregnant mothers exposed to PAH in air
- 100% exposed to chlorpyrifos and other pesticides in air
- >40% of mothers and newborns exposed to second hand smoke

Biomarkers:

- PAH-DNA adducts detected in 40% of maternal and newborn (cord) bloods
- Chlorpyrifos detected in 70-75% of maternal and cord blood samples.
- Cotinine detected in 45-50% of cord blood samples
- BPA in >90% maternal urine during pregnancy
- Phthalates in 84-100% maternal urine

Prenatal Exposures Adversely Affect Fetal and Child Development

• PAH or PAH-DNA adducts associated with:
  – Reduction in birth weight and/or head circumference
  – Developmental deficits in infancy and childhood
  – Attentional/behavioral problems in children
  – Reduced IQ
  – Increased risk of asthma and obesity
  – Epigenetic changes in cord blood

• Chlorpyrifos associated with:
  – Lower birth weight
  – Developmental deficits, ADHD, decreased IQ AND brain anomalies by MRI

• ETS associated with:
  – Reduction in birth weight
  – Developmental deficits, ADHD
  – Asthma

Prenatal BPA and Phthalates

BPA and Phthalates associated with:

- childhood eczema, airway inflammation, and/or asthma [Just et al., 2012; Donohue et al., subm.]

BPA

Butyl benzyl phthalate (BBzP)
Partnership with community organizations (WEACT and others)

Outreach to community and to policymakers

“Healthy Home Healthy Child Campaign”

IPM intervention in cohort and in NYC to reduce pesticide exposure

Monitoring of regulations

http://www.ccceh.org
GOOD NEWS

Decline in CPF levels in cord blood (pg/g) (N=395)*

*EPA Ban on residential use of chlorpyrifos took effect in 2001

[Whyatt et al., 2003]

Personal Prenatal Exposure to PAH in the NYC Cohort Declined from 1998 to 2006

[Narvaez, et al. 2008]
SUMMARY

• The fetal period is a window of heightened susceptibility

• Prenatal exposures are associated with reduced fetal growth, and developmental impairment (and other effects)

• Early interventions work

• Identification of risks from early life environmental exposures is key to prevention of disease and impairment:
  
  - in childhood
  - adolescence
  - adulthood
  - future generations
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Prenatal exposure can alter methylation as methylation marks are being established.

[Perera and Herbstman, Reprod. Tox. 2011]